PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
9541.001-304		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/SG 03/00071	03.04.2003	03.04.2003
International Patent Classification (IPC) or both national classification and IPC		
A61K35/78		
Applicant		
MEDIGEN BIOTECHNOLOGY SINGAPORE PTE. LTD.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30.10.2004 29	29.08.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Thalmair-De Meyere, Telephone No. +49 89 2399-2177

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/SG 03/00071

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-11 as originally filed

Claims, Numbers

1-38 received on 03.11.2004 with letter of 29.10.2004

Drawings, Sheets

1/3-3/3 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 4,6,7

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☒ the claims, or said claims Nos. 4,6,7 are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/ or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2,5,11-36
	No:	Claims	1,3,8-10
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-3,5,8-36
Industrial applicability (IA)	Yes:	Claims	1-38
	No:	Claims	

2. Citations and explanations

see separate sheet

Section III

The amendments filed with the letter dated 29.10.04. introduce subject-matter which extends beyond the content of the application as filed, contrary to Article 34(2)(b) PCT. The amendments concerned are the numbers 56 % in claim 4, 1 % in claim 6 and 40 % in claim 7.

Section V

The documents are numbered in the order of their citation in the corresponding International Search Report. If not indicated otherwise, it is referred to the passages cited therein.
D 1 discloses a Chinese medicine xiangshen injection with therapeutic effect for curing malignant tumor using fresh stem and leaf of pelargonium graveolens, adding flavescent sophora root powder into the geranium oil, heating and refluxing to obtain flavescent sophora essential oil, then slowly adding Tween- 80 and 5% glucose injection, grinding, filtering, filling, sealing and sterilizing so as to obtain the finished product. This disclosure takes the novelty of the subject-matter of claims 1, 3, 8, 9, 10 away. With respect to the ambiguity concerning the botanical names of rose-scented geranium (*Pelargonium* species), see especially **D 9** (Rajeswara Rao, 2000).
D 2 reports on a Chinese medicine for curing cancer in the form of soft capsules including geranium oil 350-450 (by weight portion), flavescent sophora root (300-400), gelatin and glycerin. This disclosure deprives the subject-matter of claims 1, 3, 8 of its novelty.
Hence, in summary, the subject-matter of claims 1, 3, 8-10 does not appear to be novel in view of the disclosure of either D 1 or D 2.
Furthermore, the subject-matter of claims 2 and 5 is considered as obvious to the skilled person as mere result of optimization in respect of amounts of a formulation which falls under the routine capacities of the average skilled person.
With regard to the species *P. terebinthinceum* of claim 11, Applicant is asked to provide evidence that this designation is a real commonly known name for a Pelargonium species.

Furthermore, the subject-matter of claims 12-36 does not seem to involve inventive merits for the following reasons.
D 3 shows processes for culturing tissues of a pea family plant (e.g. *Sophora subprostata* or *S. flavescens*) and obtaining an extract containing antiulcer components such as matrine

and/or oxymatrine.

D 4 reports on a composition for treating and preventing cancer made from Chinese medicinal herbs containing 42 mg of *Sophora tonkinensis*.

D 5 shows a preparation of anti-cancer medicine using sophocarpine extracted from *Sophora alopecuroides* (its portion on the ground) and made into injection, tablet, capsule and other preparations.

Hence, it was already known to the public that extractions from *Sophora* are useful for treating and preventing cancer as well as that medicine exists for curing cancer including geranium oil (D 2) and flavescent sophora root powder (D 1). Therefore, it is not surprising for the skilled person that a combination of geranium oil and extractions from the roots of Sophora tonkinensis are effective for the treatment of bone marrow suppression resulting from one or more cancer treatments.

CLAIMS

1. A composition comprising geranium oil and extractions from the root of *Sophora tonkinesis*.

2. The composition of claim 1, wherein the geranium oil and extractions from the root of *Sophora tonkinesis* have a weight ratio of about 30:1.

3. The composition of claim 1, wherein the composition comprises a mixture of powders of geranium oil and powders of extractions from the root of *Sophora tonkinesis*.

4. The composition of claim 3, wherein the powders of geranium oil is about 56% of the mixture of powders.

5. The composition of claim 4, wherein the powders of geranium oil comprise geranium oil at about 31% by weight and excipients at about 69% by weight.

6. The composition of claim 3, wherein the powders of extractions from the root of *Sophora tonkinesis* is about 1% of the mixture of powders.

7. The composition of claim 6, wherein the powders of extractions from the root of *Sophora tonkinesis* comprises *Sophora tonkinesis* extractions at about 60% by weight and excipients at about 40% by weight.

8. The composition of claim 1, wherein the geranium oil is extracted from one or more species of the genus Pelargonium.

9. The composition of claim 1, wherein the geranium oil is extracted from a plant of the genus Pelargonium and species graveolens.

10. The composition of claim 1, wherein the geranium oil is extracted from a plant of the genus Pelargonium and species roseum.

11. The composition of claim 1, wherein the geranium oil is extracted from a plant of the genus Pelargonium and species terebinthinceum.

12. Use of a composition comprising geranium oil and extractions from the roots of *Sophora tonkinesis* for the manufacture of a medicament for the treatment of bone marrow suppression resulting from one or more cancer treatments.

13. Use of a composition comprising citronellol, geraniol, geranyl formate, citronellyl formate, matrine, and oxymatrine for the manufacture of a medicament for the treatment of bone marrow suppression resulting from one or more cancer treatments.

14. Use of a composition comprising citronellol, geraniol, geranyl formate, citronellyl formate, linalool, trans-rose oxide, cis-rose oxide, matrine, oxymatrine, and sophocarpine for the manufacture of a medicament for the treatment of bone marrow suppression resulting from one or more cancer treatments.

15. Use of a composition comprising geranium oil, matrine, and oxymatrine for the manufacture of a medicament for the treatment of bone marrow suppression resulting from one or more cancer treatments.

16. Use of a composition comprising extractions from the root of *Sophora tonkinesis*, citronellol, geraniol, citronellyl formate, and geranyl formate for the manufacture of a medicament for the treatment of bone marrow suppression resulting from one or more cancer treatments.

17. The use of claim 12, wherein the bone marrow suppression is a reduction in the number of one or more types of blood cells selected from the group consisting of leukocytes, erythrocytes, and platelets.

18. The use of claim 12, wherein the one or more cancer treatments is chemotherapy, radiation therapy, or both chemotherapy and radiation therapy.

19. The use of claim 18, wherein the chemotherapy agent is 5-fluorouracil,

doxorubincin, or both 5-fluorouracil and doxorubincin.

20. The use of claim 12, wherein the treatment of bone marrow suppression is carried out through oral administration, intraperitoneal administration, or intravenous administration.

21. The use of claim 20, wherein the oral administration is carried out at a dosage in a range between about 280mg/kg/day and about 1050mg/kg/day.

22. The use of claim 21, wherein the oral administration is carried out at a dosage about 350mg/kg/day.

23. The use of claim 20, wherein the oral administration is carried out at a dosage in a range between about 1680mg/60kg/day and about 6300 mg/60kg/day.

24. The use of claim 23, wherein the oral administration is carried out at a dosage about 2100mg/60kg/day.

25. The use of claim 12, wherein the geranium oil and extractions from the root of Sophora tokinesis have a weight ratio of about 30:1.

26. The use of claim 12, wherein the treatment of bone marrow suppression is performed on humans.

27. The use of claim 20, wherein the oral administration is carried out by administering the composition in the form of powders, pastes, pills, tablets, oil capsules, syrup, liquids, or decoction soups.

28. The use of claim 20, wherein the oral administration is carried out by administering edible forms of Pelargonium plant and the root of *Sophora tonkinesis*.

29. The use of claim 12, wherein the geranium oil is extracted from one or more species of the genus Pelargonium.

30. The use of claim 12, 13, 14, 15, 16, 27, or 28, wherein the composition

further comprises a pharmaceutically acceptable solvent.

31. The use of claim 12, wherein the treatment of bone marrow suppression is carried out by administering the composition before, after, before and after, or during cancer treatments.

32. The use of claim 31, wherein the treatment of bone marrow suppression is carried out by administering the composition following a time interval between separate administrations.

33. The use of claim 32, wherein the time interval is one to fourteen days, within twenty-four hours, or within forty-eight hours.

34. Use of a composition comprising geranium oil and extractions from the roots of *Sophora tonkinesis* for the manufacture of a composition for oral consumption for preventing bone marrow suppression.

35. The use of claim 34, wherein the oral consumption is in the form of food additives, dietary supplement, or functional food.

36. Use of a composition comprising geranium oil and extractions from the roots of a Sophora plant for the manufacture of a medicament for the treatment of bone marrow suppression resulting from one or more cancer treatments.

37. The use of claim 36, wherein the Sophora plant is *Sophora alopecuroides* or *Sophora moorcroftiana*.

38. Use of a composition comprising geranium oil and extractions from the roots of *Euchresta strigillosa* for the manufacture of a medicament for the treatment of bone marrow suppression resulting from one or more cancer treatments.